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18 PULMONARY ASSESSMENT

18.1 INTRODUCTION

18.1.1 Background

Apart from irritative tracheo-bronchial symptoms occurring consequent to industrial accidents, there is no evidence that the human lung is a target organ for 2,3,7,8-tetrachlorodibenzo-p-dioxin (dioxin) toxicity. A single case of hypersensitivity pneumonitis was described in a Vietnam veteran occupationally exposed to herbicides (1). The respiratory failure that has been reported in rare cases of extreme phenoxy herbicide intoxication appears to be related to central nervous system depression rather than primary pneumotoxicity (2, 3).

Research into the pulmonary toxicity of dioxin in laboratory animals has focused on the physicochemical properties of the cytosolic aryl hydrocarbon (Ah) receptor and the carcinogenic potential of the cytochrome P-450 enzyme system in mice (4), rats (5, 6), and rabbits (7–12). Although these studies have demonstrated that dioxin enhances the activity of cytochrome P-450 and of aryl hydrocarbon hydroxylase in respiratory tract epithelium, the relevance to the development of lung disease in humans is uncertain.

Other lines of research have heightened interest in the possibility that dioxin might cause pneumotoxicity in humans. In one study (13), cytosol preparations were examined from human lung tissue specimens obtained at surgery. Only 10 of 53 specimens had detectable Ah receptors that were present at concentrations far less (10 to 30 percent) than those found in lung cytosols from laboratory animals. In mice, the induction of cytochrome P-450 enzymes by dioxin in lung was found similar to that in liver (14). In rats (15, 16), the intratracheal administration of dioxin was associated with significant dose-related increases in hepatic enzymes as well, establishing the transpulmonary absorption of dioxin and the potential for pneumotoxicity.

Lung disease has been included infrequently as a clinical endpoint in epidemiological studies of humans exposed to phenoxy herbicides. In one report (17), standard pulmonary function tests were included in clinical examinations of 367 employees 30 years after a chemical industrial explosion associated with high level exposure to 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) and, by contamination, to dioxin. Although tissue levels of dioxin were not available, 55 percent of the exposed cohorts developed chloracne, reflecting the severity of exposure. The prevalence of abnormal chest radiographs was similar in the exposed and unexposed cohorts. Significant reductions in dynamic indices of lung function were limited to cigarette smokers. In this sub-cohort, a significant reduction in forced expiratory volume at one second (FEV_1) was noted, as was a reduction in forced vital capacity (FVC). Even after adjustment for cumulative cigarette use, the predicted means for FEV_1, FVC, and the derived index, FEV_1/FVC, were significantly reduced in the exposed cohort relative to controls. These results raise the possibility that cigarette use may sensitize the lungs and make them more vulnerable as a target organ for dioxin toxicity.

In a more recent occupational morbidity study conducted by the National Institute of Occupational Safety and Health (NIOSH) (18)—one of the first to include tissue levels of dioxin in the analyses—the prevalence of two chronic pulmonary diseases, emphysema and chronic bronchitis, was determined in 281 workers exposed to dioxin for 15 years in two chemical production factories and compared with 260 unexposed controls. The clinical examination protocol was similar to the one used in the current Air Force Health Study (AFHS) and included dynamic indices of lung function (FEV_1, FVC, and FEV_1/FVC) and, on the physical examination, nine abnormalities of the thorax and lungs. These nine abnormalities were asymmetric chest excursion, abnormal chest shape, abnormal chest expansion, hyperresonant lungs, dullness to percussion, diminished breath sounds, crackles on auscultation, wheezes on auscultation, and pleural friction rub. The body burden of dioxin was determined by serum dioxin levels: mean level of 220 parts per trillion (ppt) in the exposed cohort versus 7 ppt in the controls. In contrast to the results cited above, the incidence of chronic lung disease and the prevalence of abnormal physical findings and pulmonary function tests were similar in the exposed and control groups.

Although several animal experiments have documented the occurrence of lung cancers associated with dioxin toxicity in rats (19, 20), mice (21), and monkeys (22), numerous large-scale epidemiological studies in humans exposed occupationally (23, 24), as a consequence of industrial accidents (25–27) or during military service (28–35), found no increase in the occurrence of lung cancer in populations at risk. In another large retrospective occupational study conducted by NIOSH, mortality associated with cancers of the respiratory tract was significantly increased, but only in a sub-cohort of workers with more than one year exposure and greater than 20 years of latency (36).

In one report, Marine veterans who served in Vietnam were found to be at increased risk for the development of lung cancer (37). A subsequent proportionate mortality study conducted by the Veterans' Administration reviewed the data and concluded that the apparent increase in risk might have been related to a lower than expected mortality from lung cancer in the control group of Marines who did not serve in Vietnam (38).

In the 1987 AFHS examinations, Ranch Hand participants were more likely than Comparisons to have abnormalities of the thorax and lungs (39). This finding also was seen in the 1992 examination (40). Differences between Ranch Hands and Comparisons were not seen in the laboratory measurements in 1987 or 1992. In both examinations, a slight reduction in FVC and, as a consequence, an increase in the FEV_1 to FVC ratio were noted in association with increasing serum dioxin levels. Although consistent with a subtle dose-response effect, the differences in the means were too small to be physiologically meaningful.

18.1.2 Summary of Previous Analyses of the Air Force Health Study

18.1.2.1 1982 Baseline Study Summary Results

The 1982 baseline examination explored historical pulmonary disease by questionnaire and active pulmonary function by standardized spirometric technique. These areas were of significant interest because of reported operational inhalation of Herbicide Orange by some Ranch Hand enlisted flyers and enlisted groundcrew.

The questionnaire revealed no group differences for historical diagnoses of tuberculosis and fungal infections, pneumonia, cancer, or chronic sinusitis and upper respiratory disease. At the physical examination, the Ranch Hand and Comparison unadjusted means for FEV_1 (percent predicted), FVC, and the ratio of FEV_1 to FVC were similar. Adjusted mean values were not calculated because of significant interactions (group-by-age for FEV_1 and FVC, group-by-smoking for the ratio of FEV_1 to FVC).

Exposure analyses showed two significant associations in the enlisted flyer and enlisted groundcrew strata, but neither was indicative of a linear dose-response. Attempts to adjust the means of the pulmonary function values for age and smoking revealed several interactions, but the results were essentially negative. Overall, there were no pulmonary diseases, pulmonary function data, or associations of concern.

18.1.2.2 1985 Follow-up Study Summary Results

Because of the lack of significant results from the pulmonary analyses from the baseline examination, pulmonary function (spirometric) studies were not performed during the 1985 follow-up examination. Collection of pulmonary data was limited to a questionnaire history of respiratory disease, physical examination of the thorax and lungs, and pulmonary abnormalities detected on a routine chest x ray. Mortality because of respiratory disease also was evaluated.

There were no significant group differences found for reported history of asthma, bronchitis, pleurisy, or tuberculosis based on the unadjusted analyses. Adjustments for age and lifetime smoking did not alter the findings of group similarity, although there was a significant group-by-lifetime smoking interaction for pleurisy and tuberculosis. Ranch Hands who were moderate lifetime smokers (up to 10 pack-years) had a significantly increased incidence of pleurisy and tuberculosis than did Comparisons who were moderate lifetime smokers.

Similarly, there were no significant group differences in the unadjusted analyses for the radiological and clinical respiratory findings of thorax and lungs, asymmetrical expansion, hyperresonance, dullness, wheezes, rales, and x-ray interpretations. These findings were supported by the adjusted analyses. Also, the exposure index analyses revealed no consistent dose-response pattern.

18.1.2.3 1987 Follow-up Study Summary Results

The pulmonary assessment was based on five self-reported respiratory illnesses, seven clinical observations, and eight laboratory measurements. The self-reported illnesses were based on participant-reported responses to the personal history form and the health history questionnaire. No evidence of an herbicide effect was detected in the assessment of the reported respiratory illnesses. The health of the two groups was comparable based on the clinical and laboratory variables, although Ranch Hands had a significantly higher percentage of thorax and lung abnormalities on examination than did Comparisons, based on the unadjusted analysis, and a marginally higher percentage after adjustment for covariates. No significant group differences were detected in the adjusted analyses when comparing all Ranch Hands with all Comparisons. Exploration of interactions did not reveal a consistent pattern indicating an herbicide effect. The adverse effects of smoking on pulmonary status were evident in all analyses.

18.1.2.4 Serum Dioxin Analysis of 1987 Follow-up Study Summary Results

In general, there was no association between initial dioxin levels and the discrete variables. For the continuous variables, there appeared to be a negative association with initial dioxin. The associations with current dioxin did not differ significantly between the two time strata for any of the variables. In the categorized current dioxin analyses, the percentage of abnormalities did not differ significantly among the four current dioxin categories for any of the questionnaire and physical examination variables, except under the adjusted analysis of thorax and lung abnormalities. In this case, Ranch Hands in the low and high categories had a higher percentage of abnormalities than did Comparisons in the background category; but Ranch Hands in the unknown category had a lower percentage of abnormalities than did Comparisons in the background category. For the continuous variables, the means differed among the current dioxin categories. For FVC, FEV_1, and forced expiratory flow maximum (FEFmax), the mean for the Ranch Hands in the unknown category tended to be greater than the mean for the Comparisons in the background category, but the means for the low and high categories were less than the mean for the background category. In the analysis of the ratio of observed FEV_1 to observed FVC, this trend was reversed.

In the longitudinal analysis of the ratio of observed FEV_1 to observed FVC, there was a significant positive association with current dioxin and a significant difference among the current dioxin categories, with the mean increase from 1982 to 1987 in the high category greater than the mean increase from 1982 to 1987 in the background category.

In summary, the historical, physical examination, and laboratory data analyzed in the 1987 serum dioxin follow-up study revealed no evidence for an increased occurrence of pulmonary disease in the Ranch Hand cohort in relation to the body burden of dioxin. Analysis of two laboratory variables, FVC and the ratio of observed FEV_1 to observed FVC, yielded results that were consistent with subtle dose-response effects related to the body burden of dioxin in Ranch Hands. Body habitus and, more specifically, body fat might have played a role in these associations between dioxin and pulmonary function indices.

18.1.2.5 1992 Follow-up Study Summary Results

For the medical records and physical examination pulmonary variables, the group analysis revealed significant relations for bronchitis and thorax and lung abnormalities only. For enlisted flyers, significantly more Ranch Hands than Comparisons had bronchitis and thorax and lung abnormalities. The initial dioxin, categorized dioxin, and current dioxin analyses for these variables did not confirm a dioxin dose-response relation.

For the laboratory variables, a statistically significant inverse relation was revealed between percent of predicted FVC and initial and current dioxin for Ranch Hands. When Ranch Hands were contrasted with Comparisons, no significant differences were detected. Also, the analysis of the ratio of observed FEV_1 to observed FVC within Ranch Hands revealed a significant direct relation with initial dioxin indicating that the ratio increases (becomes closer to 1) for increasing levels of initial dioxin, which may have been due to the diminishing magnitude of FVC in the denominator of the ratio.

In the longitudinal analysis of the ratio of observed FEV_1 to observed FVC, there was a significant group difference for the enlisted flyers. The Ranch Hand enlisted flyers had a larger decrease in the ratio between 1982 and 1992 than did the Comparison enlisted flyers.

In summary, the historical, physical examination, and laboratory data analyzed for this assessment revealed no consistent evidence of an increased prevalence of pulmonary disease in the Ranch Hand cohort in relation to body burden of dioxin.

18.1.3 Parameters for the 1997 Pulmonary Assessment

18.1.3.1 Dependent Variables

The pulmonary assessment was based on questionnaire, physical examination, and laboratory data collected at the 1997 follow-up examination.

18.1.3.1.1 Medical Records Data

In the self-administered family and personal history section, each study participant was asked whether he had ever experienced asthma, bronchitis, or pneumonia. The following International Classification of Diseases, 9^{th} Revision, Clinical Modification (ICD-9-CM) codes were used: asthma: 493.0–493.9; bronchitis: 466.0–466.1, 490, 491.0–491.9, 494; and pneumonia: 480.0–486, 487.0. This self-reported information was combined with information from the 1997 physical examination; the 1985, 1987, and 1992 follow-up questionnaires and physical examinations; and the baseline questionnaire and examination and, subsequently, was verified by a review of the participant's medical records. These three variables were individually analyzed as measures of the pulmonary health status of each participant.

Participants with occurrences of asthma, bronchitis, or pneumonia before duty in Southeast Asia (SEA) were excluded from the analyses of the respective variables.

18.1.3.1.2 Physical Examination Data

Part of the pulmonary assessment was based on the results of the physical examination of the thorax and lungs. A composite variable, thorax and lung abnormalities, was constructed based on the presence or absence of asymmetrical expansion, hyperresonance, dullness, wheezes, rales, or chronic obstructive pulmonary disease, as well as the physician's assessment of abnormality. This variable was coded as "abnormal" if any of these conditions was present and "normal" if none of these conditions was present. No participants were excluded for medical reasons from the analysis of this variable.

18.1.3.1.3 Laboratory Examination Data

The assessment of the laboratory examination data included the analysis of pulmonary abnormalities detected on a routine chest x ray. This variable was coded as "normal" or "abnormal." The assessment also included the analysis of pulmonary physiologic data collected during the physical examination employing standard spirometric techniques. Numerous indices were derived, including FVC—a measurement of the amount of air in liters expelled from maximum inspiration to full expiration—and FEV_1 in liters, an index derived from the FVC that quantifies the amount of air expelled at 1 second. The values used for these variables were the percentages of predicted values rather than the actual volume or flow rate. The calculations of these percentages included an adjustment for age and height, as prescribed by the American Thoracic Society. The laboratory used the same predictive values regardless of race. For these indices, lower values indicated greater compromise in the lung function. In addition, the ratio of observed FEV_1 to observed FVC was calculated as an index reflective of obstructive airway disease. These variables were analyzed as continuous variables.

Loss of vital capacity and obstructive abnormality were classified by the examiner as none, mild, moderate, or severe and were analyzed as part of the pulmonary assessment. Results judged to be between none and mild were classified as "mild" for all analyses. A similar methodology was used for results between mild and moderate (i.e., classified as "moderate") and between moderate and severe (i.e., classified as "severe"). Because of the low frequencies in the moderate and severe categories, these two categories were combined in the analysis of loss of vital capacity. No participants were excluded for medical reasons from the analysis of these variables.

As a guideline for categorizing loss of vital capacity and obstructive abnormality, the following percent reductions in the FVC and FEV_1/FVC, respectively, were used:

- Mild: 70–100%
- Moderate: 60–69%
- Moderately severe: 50–59%
- Severe: 34–49%
- Very severe: <34%.

These categorizations are based on American Thoracic Society criteria (41). The percent reductions in the FVC and the FEV_1/FVC were based on the percent of predicted values, which were adjusted for age and height.

18.1.3.2 Covariates

The effects of age, race, military occupation, current cigarette smoking (cigarettes/day), lifetime cigarette smoking history (pack-years), body fat (percent), and exposure to industrial chemicals (yes, no) were used in adjusted statistical analyses evaluating the pulmonary dependent variables. Current cigarette smoking was used as a covariate for the physical examination and laboratory variables only. The current level of cigarette smoking was not appropriate as a risk factor for an endpoint based on post-SEA history. Lifetime cigarette smoking history was used to investigate the cumulative effects of cigarette smoking on these endpoints.

Age, race, and occupation were determined from military records. Current cigarette smoking and lifetime cigarette smoking history were based on questionnaire data. For lifetime cigarette smoking history, the respondent's average smoking was estimated over his lifetime based on his responses to the 1997 questionnaire, with 1 pack-year defined as 365 packs of cigarettes smoked during a single year. The participant's lifetime exposure through 1992 to industrial chemicals was updated with information reported in the 1997 questionnaire.

Body fat was calculated from a metric body mass index (42); the formula is

$$Body\ Fat\,(in\ percent) = \frac{Weight\,(kg)}{[Height\,(m)\,]^2} \bullet 1.264 - 13.305.$$

For purposes of covariate associations for discrete dependent variables, body fat was dichotomized as "lean or normal" (≤25 percent) and "obese" (>25 percent).

18.1.4 Statistical Methods

Table 18-1 summarizes the statistical analyses performed for the pulmonary assessment. The first part of this table lists the dependent variables analyzed, source of the data, form of the data, cutpoints, covariates, and statistical methods. The second part of the table further describes the covariates. A covariate was used in its continuous form whenever possible for all adjusted analyses; if the covariate was inherently discrete (e.g., military occupation), or if a categorized form was needed to develop measures of association with the dependent variables, the covariate was categorized as shown in Table 18-1. Table 18-2 provides a summary of participants with missing dependent variable and covariate data. In addition, the number of participants excluded because of pre-SEA conditions is given.

Table 18-1. Statistical Analysis for the Pulmonary Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Asthma	MR-V	D	Yes No	(1)	(a)	U:LR A:LR
Bronchitis	MR-V	D	Yes No	(1)	(a)	U:LR A:LR
Pneumonia	MR-V	D	Yes No	(1)	(a)	U:LR A:LR

Table 18-1. Statistical Analysis for the Pulmonary Assessment (Continued)

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Thorax and Lung Abnormalities	PE	D	Yes No	(2)	None	U:LR A:LR
X-ray Interpretation	LAB	D	Abnormal Normal	(2)	None	U:LR A:LR
Forced Vital Capacity (FVC) (percent of predicted)	LAB	C	--	(2)	None	U:GLM A:GLM
Forced Expiratory Volume in 1 Second (FEV_1) (percent of predicted)	LAB	C	--	(2)	None	U:GLM A:GLM
Ratio of Observed FEV_1 to Observed FVC	LAB	C	--	(2)	None	U:GLM A:GLM L:GLM
Loss of Vital Capacity	LAB	D	Moderate/Severe Mild None	(2)	None	U:PR A:PR
Obstructive Abnormality	LAB	D	Severe Moderate Mild None	(2)	None	U:PR A:PR

[a]Covariates:
(1): age, race, military occupation, lifetime cigarette smoking history, body fat, exposure to industrial chemicals.
(2): age, race, military occupation, current cigarette smoking, lifetime cigarette smoking history, body fat, exposure to industrial chemicals.

[b]Exclusions:
(a): participants with a pre-SEA history of the disorder.

Covariates

Variable (Units)	Data Source	Data Form	Cutpoints
Age (years)	MIL	D/C	Born≥1942 Born<1942
Race	MIL	D	Black Non-Black
Occupation	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Current Cigarette Smoking (cigarettes/day)	Q-SR	D/C	0-Never 0-Former >0–20 >20
Lifetime Cigarette Smoking History (pack-years)	Q-SR	D/C	0 >0–10 >10

Table 18-1. Statistical Analysis for the Pulmonary Assessment (Continued)

Variable (Units)	Data Source	Data Form	Cutpoints
Body Fat (percent)	PE	D/C	Lean or Normal: ≤25% Obese: >25%
Industrial Chemicals Exposure	Q-SR	D	Yes No

Abbreviations

Data Source:
LAB: 1997 laboratory results
MIL: Air Force military records
MR-V: Medical records (verified)
PE: 1997 physical examination
Q-SR: Health questionnaires (self-reported)

Data Form:
C: Continuous analysis only
D: Discrete analysis only
D/C: Appropriate form for analysis (either discrete or continuous)

Statistical Analysis:
U: Unadjusted analysis
A: Adjusted analysis
L: Longitudinal analysis

Statistical Methods:
GLM: General linear models analysis
LR: Logistic regression analysis
PR: Polytomous logistic regression analysis

Table 18-2. Number of Participants Excluded or with Missing Data for the Pulmonary Assessment

		Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
Variable	Variable Use	Ranch Hand	Comparison	Initial	1987	Ranch Hand	Comparison
X-ray Interpretation	DEP	2	0	2	2	2	0
FVC	DEP	1	2	1	1	1	2
FEV_1	DEP	1	2	1	1	1	2
Ratio of the Observed FEV_1 to Observed FVC	DEP	1	2	1	1	1	2
Loss of Vital Capacity	DEP	1	2	1	1	1	2
Obstructive Abnormality	DEP	1	2	1	1	1	2
Current Cigarette Smoking	COV	1	0	0	1	1	0
Lifetime Cigarette Smoking History	COV	2	1	1	2	2	1
Pre-SEA Asthma	EXC	11	5	7	11	11	5
Pre-SEA Bronchitis	EXC	24	27	15	24	24	25
Pre-SEA Pneumonia	EXC	44	47	24	44	44	45

Table 18-2. Number of Participants Excluded or with Missing Data for Pulmonary Assessment (Continued)

Note: DEP = Dependent variable.
COV = Covariate.
EXC = Exclusion.
870 Ranch Hands and 1,251 Comparisons.
482 Ranch Hands for initial dioxin; 863 Ranch Hands for 1987 dioxin.
863 Ranch Hands and 1,213 Comparisons for categorized dioxin.

18.1.4.1 Longitudinal Analysis

Longitudinal analyses were performed to evaluate associations between group or dioxin and the change in the ratio of observed FEV_1 to observed FVC between the 1982 baseline examination and the 1997 follow-up.

18.2 RESULTS

18.2.1 Dependent Variable-Covariate Associations

Covariate tests of association were performed to examine the relations between the covariates used in the adjusted analyses and the dependent variables. Appendix F, Table F-10, provides summary results of these analyses to test the statistical significance of the associations. These associations are pairwise between the dependent variable and the covariate and are not adjusted for any other covariates. Participants with a pre-SEA occurrence of asthma were excluded from the analysis of asthma, and similar exclusions were made for bronchitis and pneumonia. Statistically significant associations are discussed below.

Covariate tests of association revealed no significant relations between asthma and any of the covariates ($p>0.70$ for all tests).

Analysis of bronchitis revealed significant covariate associations with lifetime cigarette smoking history ($p=0.002$) and industrial chemicals exposure ($p=0.009$), and a marginally significant association with race ($p=0.069$). The prevalence of bronchitis increased as lifetime cigarette smoking history increased. Participants who were exposed to industrial chemicals had a higher prevalence of bronchitis than those who were not exposed (22.0% vs. 17.2%). Non-Black participants had a higher prevalence of bronchitis than did Black participants (20.6% vs. 13.5%).

Covariate association tests for pneumonia revealed significant associations with age ($p=0.002$) and lifetime cigarette smoking history ($p=0.037$). Older participants had a higher percentage of pneumonia than did the younger participants (13.1% vs. 8.6%). Participants with greater than 10 pack-years had the highest prevalence of pneumonia (13.0%), followed by nonsmokers (9.6%) and participants between 0 and 10 pack-years (9.3%).

Tests of covariate association for thorax and lung abnormalities showed age ($p=0.001$), race ($p=0.042$), occupation ($p=0.001$), current cigarette smoking ($p=0.001$), lifetime cigarette smoking history ($p=0.001$), and body fat ($p=0.047$) to be significant. Exposure to industrial chemicals showed a marginally significant association with thorax and lung abnormalities ($p=0.062$). Older participants had a higher percentage of thorax and lung abnormalities (13.6%) than did the younger participants (8.6%). Non-Blacks had a higher prevalence of thorax and lungs abnormalities (11.8%) than did Blacks (5.5%). Enlisted flyers had the highest prevalence of abnormalities of the thorax and lung (18.6%), followed by enlisted groundcrew (12.1%) and officers (7.7%). For both current cigarette smoking and lifetime cigarette smoking history, the prevalence of thorax and lung abnormalities increased as smoking increased. Participants with normal body fat had a higher percentage of thorax and lung abnormalities than obese participants (12.3% vs. 9.2%). Participants who had been exposed to industrial chemicals had a higher percentage of thorax and lung abnormalities (12.5%) than did participants who had not been exposed to industrial chemicals (9.7%).

Covariate association tests for the interpretation of the chest x ray revealed significant associations with age and lifetime cigarette smoking history (p=0.018 for both). Older participants had a higher percentage of x-ray interpretations showing abnormalities than did the younger participants (11.6% vs. 8.4%). The prevalence of x-ray interpretations showing abnormalities increased as lifetime cigarette smoking history increased.

For both current cigarette smoking and lifetime cigarette smoking history, FVC decreased significantly as smoking increased (p=0.002 for current cigarette smoking and p<0.001 for lifetime cigarette smoking history). FVC decreased significantly as body fat increased (p<0.001). Black participants had a lower mean FVC than did non-Black participants (87.84 vs. 99.81 percent of predicted, p<0.001). Occupation showed a significant association with FVC (p=0.005). Enlisted groundcrew had the lowest mean FVC (97.99 percent), followed by enlisted flyers (99.22 percent) and officers (100.28 percent).

FEV_1 decreased significantly with age (p<0.001), current cigarette smoking (p<0.001), lifetime cigarette smoking history (p<0.001), and body fat (p=0.001). Black participants had a lower mean FEV_1 than did non-Black participants (86.63 vs. 94.71 percent of predicted, p<0.001). Occupation showed a significant association with FEV_1 (p=0.002). Enlisted flyers had the lowest mean FEV_1 (91.76 percent), followed by enlisted groundcrew (93.90 percent) and officers (95.57 percent). The association between FEV_1 and exposure to industrial chemicals was marginally significant (p=0.092). The mean FEV_1 for participants not exposed to industrial chemicals was 95.04 percent, whereas the mean FEV_1 for participants exposed to industrial chemicals was 93.72 percent.

Because of the distribution of the data, a natural logarithm transformation of 1.0 minus the ratio of the observed FEV_1 to the observed FVC ratio was used. Because of this transformation, a negative correlation implies a positive association between dioxin and the ratio. The ratio of the observed FEV_1 to the observed FVC displayed significant associations with age, race, occupation, current cigarette smoking, lifetime cigarette smoking history, and body fat (p<0.001 for each). The ratio decreased with age, current cigarette smoking, and lifetime cigarette smoking history, but increased as body fat increased. Black participants had a higher mean ratio of the observed FEV_1 to the observed FVC than did non-Black participants (0.791 vs. 0.760). Enlisted groundcrew had the highest mean ratio (0.771), followed by officers (0.759) and enlisted flyers (0.745).

Tests of covariate association for loss of vital capacity showed a significant association with age (p=0.031), race (p=0.001), body fat (p=0.001), and lifetime cigarette smoking history (p=0.029). The association between loss of vital capacity and exposure to industrial chemicals was marginally significant (p=0.064). A higher percentage of older participants had a mild loss of vital capacity and a moderate or severe loss of vital capacity (mild: 8.4%, moderate or severe: 1.9%) than did younger participants (mild: 7.0%, moderate or severe: 0.8%). A higher percentage of Black participants had a mild loss of vital capacity and a moderate or severe loss of vital capacity (mild: 17.2%, moderate or severe: 4.7%) than did non-Blacks (mild: 7.2%, moderate or severe: 1.2%). Obese participants had a higher percentage of loss of vital capacity (mild: 11.9%, moderate or severe: 2.3%) than did those with normal body fat (mild: 6.1%, moderate or severe: 1.1%). Results also indicate that the percentage of mild loss of vital capacity and a moderate or severe loss of vital capacity increased as the number of pack-years increased. A higher percentage of participants exposed to industrial chemicals had a mild and moderate or severe loss of vital capacity (mild: 8.5%, moderate or severe: 1.7%) than did participants not exposed to industrial chemicals (mild: 6.6%, moderate or severe: 0.9%).

Covariate analysis with obstructive abnormality revealed significant associations with age, occupation, current cigarette smoking, and lifetime cigarette smoking history (p=0.001 for each). Older participants had a higher percentage of obstructive abnormalities (mild: 37.1%, moderate: 8.6%, severe: 2.2%) than did younger participants (mild: 21.9%, moderate: 2.6%, severe: 0.4%). Enlisted flyers had a higher percentage of obstructive abnormalities than did officers or enlisted groundcrew. The percentage of obstructive abnormalities increased as the number of cigarettes smoked per day increased and as the number of pack-years increased.

18.2.2 Exposure Analysis

The following section presents results of the statistical analyses of the dependent variables shown in Table 18-1. Asthma, bronchitis, and pneumonia were derived from self-reported responses and verified by a medical records review. Additional dependent variables were taken from results of the physical examination and laboratory portions of the 1997 follow-up examination.

Four models were examined for each dependent variable given in Table 18-1. The analyses of these models are presented below. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7, respectively. These analyses were performed both unadjusted and adjusted for relevant covariates. Model 1 examined the relation between the dependent variable and group (i.e., Ranch Hand or Comparison). In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure. As an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each occupational category (i.e., officers, enlisted flyers, and enlisted groundcrew). As described in previous reports and Table 2-8, the average levels of exposure to dioxin were highest for enlisted groundcrew, followed by enlisted flyers, then officers.

Model 2 explored the relation between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. If a participant did not have a 1987 dioxin level, the 1992 level was used to estimate the initial dioxin level. If a participant did not have a 1987 or a 1992 dioxin level, the 1997 level was used to estimate the initial dioxin level. A statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin was included in this model to account for body-fat-related differences in elimination rate (43).

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories are referred to as "low Ranch Hand" and "high Ranch Hand." Two additional categories, Ranch Hands with 1987 serum dioxin levels at or below 10 ppt and Comparisons with 1987 serum dioxin levels at or below 10 ppt, were formed and included in the model. Ranch Hands with 1987 serum dioxin levels at or below 10 ppt are referred to as the "background Ranch Hand" category. Dioxin levels in 1992 were used if the 1987 level was not available, and dioxin levels in 1997 were used if the 1987 and 1992 levels were not available. These four categories—Comparisons, background Ranch Hands, low Ranch Hands, and high Ranch Hands—were used in Model 3 analyses. The relation between the dependent variable in each of the three Ranch Hand categories and the dependent variable in the Comparison category was examined. A fourth contrast, exploring the relation of the dependent variable in the combined low and high Ranch Hand categories relative to Comparisons, also was conducted. This combination is referred to in the tables as the "low plus high Ranch Hand" category. As in Model 2, a statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin was included in this model.

Model 4 examined the relation between the dependent variable and 1987 lipid-adjusted dioxin levels in all Ranch Hands with a dioxin measurement. If a participant did not have a 1987 dioxin measurement, the 1992 measurement was used to determine the dioxin level. If a participant did not have a 1987 or a 1992 dioxin measurement, the 1997 measurement was used to determine the dioxin level.

18.2.2.1   Medical Records Variables

18.2.2.1.1 Asthma

All unadjusted and adjusted analyses of asthma for Models 1 through 4 were nonsignificant (Table 18-3(a–h): p>0.11 for all analyses).

Table 18-3. Analysis of Asthma

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***41 (4.8)***	***1.37 (0.89,2.11)***	***0.158***
	Comparison	***1,246***	***44 (3.5)***		
Officer	Ranch Hand	338	18 (5.3)	1.57 (0.80,3.10)	0.191
	Comparison	492	17 (3.5)		
Enlisted Flyer	Ranch Hand	149	3 (2.0)	0.46 (0.12,1.76)	0.257
	Comparison	187	8 (4.3)		
Enlisted Groundcrew	Ranch Hand	372	20 (5.4)	1.64 (0.86,3.11)	0.132
	Comparison	567	19 (3.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.36 (0.87,2.10)***	***0.175***
Officer	1.48 (0.74,2.94)	0.266
Enlisted Flyer	0.45 (0.12,1.74)	0.247
Enlisted Groundcrew	1.69 (0.89,3.21)	0.111

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	**n**	**Number (%) Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	156	8 (5.1)	1.18 (0.86,1.62)	0.318
Medium	161	4 (2.5)		
High	158	9 (5.7)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 18-3. Analysis of Asthma (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
474	1.22 (0.82,1.82)	0.328

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	**n**	**Number (%) Yes**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,208	42 (3.5)		
Background RH	377	19 (5.0)	1.47 (0.84,2.58)	0.174
Low RH	235	10 (4.3)	1.23 (0.61,2.50)	0.559
High RH	240	11 (4.6)	1.33 (0.67,2.64)	0.408
Low plus High RH	475	21 (4.4)	1.28 (0.75,2.19)	0.363

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,207		
Background RH	376	1.52 (0.86,2.70)	0.149
Low RH	234	1.13 (0.54,2.36)	0.753
High RH	240	1.29 (0.64,2.61)	0.479
Low plus High RH	474	1.21 (0.69,2.10)	0.506

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 18-3. Analysis of Asthma (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	285	12 (4.2)	1.06 (0.86,1.31)	0.594
Medium	282	15 (5.3)		
High	285	13 (4.6)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
Analysis Results for Log_2 (1987 Dioxin + 1)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
850	1.06 (0.81,1.37)	0.680

[a] Relative risk for a twofold increase in 1987 dioxin.

18.2.2.1.2 Bronchitis

The unadjusted and adjusted Model 1 analyses of bronchitis showed no difference between Ranch Hands and Comparisons when all occupations were combined (Table 18-4(a,b): p=0.177, unadjusted; p=0.213, adjusted). After stratifying by occupation, a marginally significant association was revealed between enlisted flyer Ranch Hands and enlisted flyer Comparisons in both the unadjusted and adjusted analyses (Table 18-4(a,b): Est. RR=1.63, p=0.066, for the unadjusted analysis; Adj. RR=1.61, p=0.075, for the adjusted analysis). The percentage of Ranch Hand enlisted flyers with bronchitis was 27.8, as compared to 19.1 percent of the Comparison enlisted flyers. Contrasts of Ranch Hands and Comparisons in the other occupations were nonsignificant (Table 18-4(a,b): p>0.49 for all analyses).

Table 18-4. Analysis of Bronchitis

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***846***	***183 (21.6)***	***1.16 (0.94,1.44)***	***0.177***
	Comparison	***1,224***	***235 (19.2)***		
Officer	Ranch Hand	329	60 (18.2)	1.03 (0.71,1.48)	0.886
	Comparison	482	86 (17.8)		
Enlisted Flyer	Ranch Hand	144	40 (27.8)	1.63 (0.97,2.73)	0.066
	Comparison	183	35 (19.1)		
Enlisted Groundcrew	Ranch Hand	373	83 (22.3)	1.12 (0.81,1.54)	0.496
	Comparison	559	114 (20.4)		

Table 18-4. Analysis of Bronchitis (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	**Adjusted Relative Risk (95% C.I.)**	**p-Value**
All	***1.15 (0.92,1.43)***	***0.213***
Officer	1.02 (0.70,1.47)	0.936
Enlisted Flyer	1.61 (0.95,2.71)	0.075
Enlisted Groundcrew	1.11 (0.81,1.54)	0.514

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Number (%) Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	150	33 (22.0)	1.06 (0.89,1.25)	0.513
Medium	161	29 (18.0)		
High	156	36 (23.1)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
466	1.07 (0.88,1.30)	0.510

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	**n**	**Number (%) Yes**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,188	230 (19.4)		
Background RH	372	84 (22.6)	1.22 (0.92,1.62)	0.174
Low RH	228	44 (19.3)	1.00 (0.70,1.43)	0.980
High RH	239	54 (22.6)	1.21 (0.87,1.70)	0.262
Low plus High RH	467	98 (21.0)	1.10 (0.84,1.44)	0.479

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 18-4. Analysis of Bronchitis (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,187		
Background RH	371	1.31 (0.98,1.75)	0.073
Low RH	227	0.94 (0.65,1.36)	0.734
High RH	239	1.10 (0.78,1.56)	0.584
Low plus High RH	466	1.02 (0.78,1.34)	0.891

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log$_2$ (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) Yes**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	282	63 (22.3)	0.97 (0.87,1.08)	0.579
Medium	274	56 (20.4)		
High	283	63 (22.3)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
Analysis Results for Log$_2$ (1987 Dioxin + 1)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
837	0.90 (0.79,1.03)	0.137

[a] Relative risk for a twofold increase in 1987 dioxin.

Models 2 and 4 showed no significant associations between dioxin and bronchitis (Table 18-4(c,d,g,h): p>0.13 for all analyses).

The unadjusted Model 3 analysis results of bronchitis were nonsignificant (Table 18-4(e): p>0.17 for each contrast). Adjusting for covariates revealed a marginally significant difference between Ranch Hands in the background dioxin category and Comparisons (Table 18-4(f): Adj. RR=1.31, p=0.073). The percentage of Ranch Hands with bronchitis in the background dioxin category was 22.6, versus 19.4 percent in the Comparison category.

18.2.2.1.3 Pneumonia

All unadjusted and adjusted Models 1, 3, and 4 analyses of pneumonia showed no significant results (Table 18-5(a,b,e–h): p>0.10 for all analyses).

Table 18-5. Analysis of Pneumonia

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***826***	***85 (10.3)***	***0.87 (0.66,1.16)***	***0.344***
	Comparison	***1,204***	***140 (11.6)***		
Officer	Ranch Hand	322	34 (10.6)	0.75 (0.48,1.17)	0.200
	Comparison	470	64 (13.6)		
Enlisted Flyer	Ranch Hand	139	19 (13.7)	1.74 (0.85,3.57)	0.129
	Comparison	180	15 (8.3)		
Enlisted Groundcrew	Ranch Hand	365	32 (8.8)	0.78 (0.50,1.22)	0.271
	Comparison	554	61 (11.0)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.87 (0.66,1.16)***	***0.354***
Officer	0.74 (0.47,1.16)	0.185
Enlisted Flyer	1.75 (0.85,3.61)	0.126
Enlisted Groundcrew	0.79 (0.50,1.24)	0.304

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	**n**	**Number (%) Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	147	21 (14.3)	0.81 (0.63,1.05)	0.097
Medium	156	12 (7.7)		
High	155	13 (8.4)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
457	0.85 (0.63,1.14)	0.274

[a] Relative risk for a twofold increase in initial dioxin.

Table 18-5. Analysis of Pneumonia (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	**n**	**Number (%) Yes**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,168	134 (11.5)		
Background RH	361	38 (10.5)	0.93 (0.63,1.36)	0.708
Low RH	222	27 (12.2)	1.06 (0.68,1.65)	0.790
High RH	236	19 (8.1)	0.66 (0.40,1.09)	0.107
Low plus High RH	458	46 (10.0)	0.83 (0.58,1.19)	0.315

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,167		
Background RH	360	0.90 (0.61,1.33)	0.602
Low RH	221	0.98 (0.63,1.54)	0.929
High RH	236	0.74 (0.44,1.25)	0.265
Low plus High RH	457	0.85 (0.59,1.23)	0.386

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) Yes**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	269	29 (10.8)	0.91 (0.78,1.07)	0.236
Medium	270	33 (12.2)		
High	280	22 (7.9)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 18-5. Analysis of Pneumonia (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
817	0.89 (0.73,1.08)	0.229

[a] Relative risk for a twofold increase in 1987 dioxin.

The unadjusted Model 2 analysis found a marginally significant relation between pneumonia and initial dioxin (Table 18-5(c): Est. RR=0.81, p=0.097). As initial dioxin increased, the prevalence of pneumonia decreased. The percentages of Ranch Hands with pneumonia in the low, medium, and high initial dioxin categories were 14.3, 7.7, and 8.4, respectively. After adjustment for covariates, the association was nonsignificant (Table 18-5(d): p=0.274).

18.2.2.2 Physical Examination Variable

18.2.2.2.1 Thorax and Lung Abnormalities

Results from the unadjusted and adjusted Models 1 through 3 analyses of thorax and lung abnormalities were nonsignificant (Table 18-6(a–f): p≥0.11 for each analysis).

Table 18-6. Analysis of Thorax and Lung Abnormalities

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***870***	***102 (11.7)***	***1.05 (0.80,1.38)***	***0.704***
	Comparison	***1,251***	***140 (11.2)***		
Officer	Ranch Hand	341	31 (9.1)	1.40 (0.84,2.33)	0.200
	Comparison	494	33 (6.7)		
Enlisted Flyer	Ranch Hand	151	29 (19.2)	1.07 (0.62,1.85)	0.810
	Comparison	187	34 (18.2)		
Enlisted Groundcrew	Ranch Hand	378	42 (11.1)	0.85 (0.57,1.27)	0.434
	Comparison	570	73 (12.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.97 (0.71,1.31)***	***0.821***
Officer	1.57 (0.90,2.71)	0.110
Enlisted Flyer	0.99 (0.53,1.85)	0.978
Enlisted Groundcrew	0.69 (0.44,1.09)	0.115

Table 18-6. Analysis of Thorax and Lung Abnormalities (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	**n**	**Number (%) Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	160	22 (13.8)	1.06 (0.86,1.31)	0.573
Medium	162	23 (14.2)		
High	160	17 (10.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
481	1.14 (0.86,1.51)	0.366

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,213	137 (11.3)		
Background RH	381	39 (10.2)	0.82 (0.56,1.20)	0.304
Low RH	239	31 (13.0)	1.19 (0.79,1.82)	0.408
High RH	243	31 (12.8)	1.24 (0.82,1.89)	0.313
Low plus High RH	482	62 (12.9)	1.22 (0.88,1.68)	0.232

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 18-6. Analysis of Thorax and Lung Abnormalities (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,212		
Background RH	380	0.84 (0.55,1.28)	0.412
Low RH	238	1.01 (0.63,1.62)	0.953
High RH	243	1.01 (0.62,1.64)	0.977
Low plus High RH	481	1.01 (0.70,1.46)	0.955

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for $\mathbf{Log_2}$ (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) Yes**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	288	32 (11.1)	1.03 (0.90,1.19)	0.653
Medium	287	31 (10.8)		
High	288	38 (13.2)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
Analysis Results for $\mathbf{Log_2}$ (1987 Dioxin + 1)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
861	1.20 (1.00,1.43)	0.054

[a] Relative risk for a twofold increase in 1987 dioxin.

The unadjusted Model 4 analysis was nonsignificant (Table 18-6(g): p=0.653). After adjusting for covariates, a marginally significant association between thorax and lung abnormalities and 1987 dioxin was revealed (Table 18-6(h): Adj. RR=1.20, p=0.054). As 1987 dioxin increased, the prevalence of thorax and lung abnormalities increased. The percentages of Ranch Hands with thorax and lung abnormalities in the low, medium, and high 1987 dioxin categories were 11.1, 10.8, and 13.2, respectively.

18.2.2.3 Laboratory Examination Variables

18.2.2.3.1 X-ray Interpretation

All unadjusted and adjusted analyses of the chest x-ray interpretation for Models 1 and 2 were nonsignificant (Table 18-7(a–d): p>0.15 for each analysis).

Table 18-7. Analysis of X-ray Interpretation

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***868***	***98 (11.3)***	***1.22 (0.92,1.62)***	***0.166***
	Comparison	***1,251***	***118 (9.4)***		
Officer	Ranch Hand	341	39 (11.4)	1.39 (0.88,2.20)	0.160
	Comparison	494	42 (8.5)		
Enlisted Flyer	Ranch Hand	151	16 (10.6)	1.19 (0.58,2.43)	0.643
	Comparison	187	17 (9.1)		
Enlisted Groundcrew	Ranch Hand	376	43 (11.4)	1.12 (0.74,1.70)	0.599
	Comparison	570	59 (10.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.23 (0.92,1.64)***	***0.158***
Officer	1.39 (0.87,2.20)	0.167
Enlisted Flyer	1.16 (0.56,2.39)	0.685
Enlisted Groundcrew	1.14 (0.75,1.73)	0.554

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	**n**	**Number (%) Abnormal**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	160	18 (11.3)	0.89 (0.70,1.15)	0.373
Medium	161	14 (8.7)		
High	159	11 (6.9)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 18-7. Analysis of X-ray Interpretation (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
479	0.95 (0.71,1.27)	0.730

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,213	116 (9.6)		
Background RH	381	53 (13.9)	1.56 (1.10,2.21)	0.013
Low RH	239	26 (10.9)	1.15 (0.73,1.80)	0.546
High RH	241	17 (7.1)	0.70 (0.41,1.20)	0.196
Low plus High RH	480	43 (9.0)	0.90 (0.62,1.31)	0.576

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,212		
Background RH	380	1.69 (1.18,2,43)	0.004
Low RH	238	1.11 (0.70,1.75)	0.657
High RH	241	0.66 (0.38,1.13)	0.127
Low plus High RH	479	0.85 (0.58,1.24)	0.406

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 18-7. Analysis of X-ray Interpretation (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	37 (12.8)	0.83 (0.71,0.97)	0.015
Medium	287	39 (13.6)		
High	286	20 (7.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
Analysis Results for Log_2 (1987 Dioxin + 1)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
859	0.80 (0.67,0.96)	0.015

[a] Relative risk for a twofold increase in 1987 dioxin.

In the Model 3 unadjusted analysis of the x-ray interpretation, a significant difference was revealed between Ranch Hands in the background dioxin category and Comparisons (Table 18-7(e): Est. RR=1.56, p=0.013). The percentage of Ranch Hands in the background dioxin category with an x ray showing abnormalities was 13.9 percent, versus 9.6 percent of Comparisons. The same contrast was significant in the adjusted analysis (Table 18-7(f): Adj. RR=1.69, p=0.004). Unadjusted and adjusted contrasts of the low, high, and low plus high dioxin Ranch Hand categories with Comparisons were all nonsignificant (Table 18-7(e,f): p>0.12 for all analyses).

Both the unadjusted and adjusted Model 4 analyses revealed significant associations between the x-ray interpretation and 1987 dioxin (Table 18-7(g,h): Est. RR=0.83, p=0.015; Adj. RR=0.80, p=0.015, respectively). As the 1987 dioxin level increased, the prevalence of an x ray showing abnormalities decreased. The percentages of participants with an x-ray interpretation showing abnormalities in the low, medium, and high 1987 dioxin categories were 12.8, 13.6, and 7.0, respectively.

18.2.2.3.2 FVC (Percent of Predicted)

All unadjusted and adjusted analyses of the FVC were nonsignificant (Table 18-8: p>0.32 for all analyses).

Table 18-8. Analysis of FVC (Percent of Predicted)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean	Difference of Means (95% C.I.)	p-Value
All	***Ranch Hand***	***869***	***99.31***	***0.38 (–0.91,1.68)***	***0.564***
	Comparison	***1,249***	***98.93***		
Officer	Ranch Hand	341	100.48	0.33 (–1.73,2.39)	0.753
	Comparison	494	100.14		
Enlisted Flyer	Ranch Hand	151	99.64	0.75 (–2.45,3.96)	0.645
	Comparison	186	98.88		
Enlisted Groundcrew	Ranch Hand	377	98.14	0.24 (–1.71,2.18)	0.811
	Comparison	569	97.90		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean	Difference of Adj. Means (95% C.I.)	p-Value
All	***Ranch Hand***	***867***	***94.21***	***0.41 (–0.81,1.64)***	***0.506***
	Comparison	***1,248***	***93.79***		
Officer	Ranch Hand	340	94.31	0.56 (–1.39,2.50)	0.575
	Comparison	494	93.76		
Enlisted Flyer	Ranch Hand	151	95.01	0.56 (–2.47,3.59)	0.716
	Comparison	186	94.45		
Enlisted Groundcrew	Ranch Hand	376	93.36	0.23 (–1.61,2.07)	0.804
	Comparison	568	93.12		

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Mean	Adj. Mean[a]	R^2	Slope (Std. Error)	p-Value
Low	160	98.34	98.13	0.018	0.332 (0.491)	0.499
Medium	161	97.80	97.76			
High	160	99.44	99.68			

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean	R^2	Adj. Slope (Std. Error)	p-Value
Low	159	95.17	0.099	–0.303 (0.558)	0.588
Medium	161	94.32			
High	160	95.09			

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 18-8. Analysis of FVC (Percent of Predicted) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	**n**	**Mean**	**Adj. Mean[a]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)**	**p-Value**
Comparison	1,211	99.09	99.14		
Background RH	381	100.18	99.33	0.19 (–1.50,1.88)	0.825
Low RH	238	98.07	98.34	–0.80 (–2.83,1.23)	0.439
High RH	243	98.97	99.79	0.66 (–1.36,2.67)	0.523
Low plus High RH	481	98.52	99.07	–0.06 (–1.61,1.48)	0.935

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	**n**	**Adj. Mean**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)**	**p-Value**
Comparison	1,210	93.87		
Background RH	380	93.72	–0.15 (–1.80,1.50)	0.859
Low RH	237	94.29	0.42 (–1.54,2.39)	0.674
High RH	243	94.61	0.75 (–1.25,2.74)	0.465
Low plus High RH	480	94.45	0.59 (–0.92,2.09)	0.445

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin +1)**		
1987 Dioxin	**n**	**Mean**	**R^2**	**Slope (Std. Error)**	**p-Value**
Low	288	100.86	0.001	–0.312 (0.338)	0.356
Medium	287	98.03			
High	287	98.86			

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 18-8. Analysis of FVC (Percent of Predicted) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean	R^2	Adjusted Slope (Std. Error)	p-Value
Low	287	94.50	0.111	0.377 (0.385)	0.329
Medium	286	94.05			
High	287	95.18			

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

18.2.2.3.3 FEV_1 (Percent of Predicted)

No significant relations were observed between group or dioxin and FEV_1 in any of the analyses (Table 18-9(a–h): $p>0.13$ for all analyses).

Table 18-9. Analysis of FEV_1 (Percent of Predicted)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean	Difference of Means (95% C.I.)	p-Value
All	***Ranch Hand***	***869***	***94.13***	***–0.15 (–1.66,1.37)***	***0.849***
	Comparison	***1,249***	***94.28***		
Officer	Ranch Hand	341	95.47	–0.18 (–2.58,2.23)	0.886
	Comparison	494	95.65		
Enlisted Flyer	Ranch Hand	151	91.09	–1.21 (–4.95,2.54)	0.527
	Comparison	186	92.30		
Enlisted Groundcrew	Ranch Hand	377	94.14	0.40 (–1.87,2.67)	0.729
	Comparison	569	93.74		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adjusted Mean	Difference of Adj. Means (95% C.I.)	p-Value
All	***Ranch Hand***	***867***	***90.23***	***0.17 (–1.24,1.57)***	***0.814***
	Comparison	***1,248***	***90.06***		
Officer	Ranch Hand	340	90.92	0.11 (–2.13,2.35)	0.925
	Comparison	494	90.81		
Enlisted Flyer	Ranch Hand	151	89.19	–1.27 (–4.75,2.21)	0.475
	Comparison	186	90.46		
Enlisted Groundcrew	Ranch Hand	376	90.07	0.75 (–1.36,2.87)	0.484
	Comparison	568	89.32		

Table 18-9. Analysis of FEV_1 (Percent of Predicted) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				**Analysis Results for Log_2 (Initial Dioxin)**		
Initial Dioxin	**n**	**Mean**	**Adj. Mean[a]**	**R^2**	**Slope (Std. Error)**	**p-Value**
Low	160	93.08	93.14	0.006	0.870 (0.581)	0.135
Medium	161	91.83	91.84			
High	160	97.27	97.20			

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)**		
Initial Dioxin	**n**	**Adj. Mean**	**R^2**	**Adj. Slope (Std. Error)**	**p-Value**
Low	159	91.50	0.143	0.007 (0.637)	0.991
Medium	161	90.10			
High	160	93.52			

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	**n**	**Mean**	**Adj. Mean[a]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)**	**p-Value**
Comparison	1,211	94.36	94.38		
Background RH	381	94.17	93.94	–0.44 (–2.46,1.57)	0.668
Low RH	238	92.82	92.89	–1.48 (–3.90,0.93)	0.229
High RH	243	95.27	95.50	1.12 (–1.28,3.53)	0.360
Low plus High RH	481	94.06	94.21	–0.17 (–2.01,1.67)	0.859

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 18-9. Analysis of FEV_1 (Percent of Predicted) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	**n**	**Adj. Mean**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)**	**p-Value**
Comparison	1,210	90.03		
Background RH	380	89.32	–0.70 (–2.59,1.19)	0.469
Low RH	237	90.58	0.55 (–1.70,2.80)	0.632
High RH	243	91.19	1.16 (–1.13,3.45)	0.319
Low plus High RH	480	90.89	0.86 (–0.86,2.58)	0.328

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin +1)**		
1987 Dioxin	**n**	**Mean**	**R^2**	**Slope (Std. Error)**	**p-Value**
Low	288	94.88	0.002	0.496 (0.402)	0.217
Medium	287	92.76			
High	287	94.69			

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**		
1987 Dioxin	**n**	**Adj. Mean**	**R^2**	**Adjusted Slope (Std. Error)**	**p-Value**
Low	287	89.98	0.161	0.652 (0.443)	0.142
Medium	286	89.99			
High	287	91.21			

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

18.2.2.3.4 Ratio of Observed FEV_1 to Observed FVC

Because of the distribution of the data, a natural logarithm transformation of 1.0 minus the ratio was used. Because of this transformation, a negative slope in Models 2 and 4 implies a positive association between dioxin and the ratio of observed FEV_1 to FVC. A negative association, which would be represented by a positive slope, is considered adverse for this variable.

Model 1 showed no significant difference between Ranch Hands and Comparisons in the mean ratio of observed FEV_1 to observed FVC (Table 18-10(a,b): p>0.36 for each contrast).

The Model 2 unadjusted analysis showed a significant positive association between the ratio of observed FEV_1 to observed FVC and initial dioxin (Table 18-10(c): slope=–0.026, p=0.023). The mean ratios in the low, medium, and high initial dioxin categories were 0.759, 0.756, and 0.783, respectively. The adjusted analysis was nonsignificant (Table 18-10(d): p=0.360).

The Model 3 unadjusted and adjusted analyses showed no significant difference between any of the Ranch Hand dioxin categories and the Comparison group (Table 18-10(e,f): p>0.16 for each contrast).

The unadjusted Model 4 analysis found a significant positive association between 1987 dioxin and the ratio of observed FEV_1 to observed FVC (slope=–0.031, p<0.001). The mean ratios in the low, medium, and high 1987 dioxin categories were 0.753, 0.757, and 0.771, respectively. After adjusting for covariates, the results were nonsignificant (p=0.161).

Table 18-10. Analysis of the Ratio of Observed FEV_1 to Observed FVC

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***869***	***0.760***	***–0.003 --***	***0.366***
	Comparison	***1,249***	***0.763***		
Officer	Ranch Hand	341	0.756	–0.005 --	0.376
	Comparison	494	0.761		
Enlisted Flyer	Ranch Hand	151	0.741	–0.007 --	0.431
	Comparison	186	0.748		
Enlisted Groundcrew	Ranch Hand	377	0.772	0.001 --	0.843
	Comparison	569	0.771		

[a] Transformed from natural logarithm scale of 1.0 – ratio.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale of 1.0 – ratio.
[c] P-value is based on difference of means on natural logarithm scale of 1.0 – ratio.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***867***	***0.770***	***–0.001 --***	***0.701***
	Comparison	***1,248***	***0.771***		
Officer	Ranch Hand	340	0.771	–0.004 --	0.411
	Comparison	494	0.775		
Enlisted Flyer	Ranch Hand	151	0.764	–0.005 --	0.486
	Comparison	186	0.770		
Enlisted Groundcrew	Ranch Hand	376	0.774	0.003 --	0.532
	Comparison	568	0.771		

[a] Transformed from natural logarithm scale of 1.0 – ratio.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale of 1.0 – ratio.
[c] P-value is based on difference of means on natural logarithm scale of 1.0 – ratio.

Table 18-10. Analysis of the Ratio of Observed FEV_1 to Observed FVC (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	160	0.757	0.759	0.053	–0.026 (0.011)	0.023
Medium	161	0.756	0.756			
High	160	0.785	0.783			

[a] Transformed from natural logarithm scale of 1.0 – ratio.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of (1.0 – ratio) versus $\log_2$ (initial dioxin); because of this transformation, a negative slope implies a positive association between the ratio and $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	159	0.773	0.216	–0.011 (0.012)	0.360
Medium	161	0.770			
High	160	0.788			

[a] Transformed from natural logarithm scale of 1.0 – ratio.
[b] Slope and standard error based on natural logarithm of (1.0 – ratio) versus $\log_2$ (initial dioxin); because of this transformation, a negative slope implies a positive association between the ratio and $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,211	0.763	0.763		
Background RH	381	0.753	0.757	–0.006 --	0.192
Low RH	238	0.759	0.757	–0.006 --	0.341
High RH	243	0.774	0.770	0.007 --	0.164
Low plus High RH	481	0.766	0.764	0.001 --	0.764

[a] Transformed from natural logarithm scale of 1.0 – ratio.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale of 1.0 – ratio.
[d] P-value is based on difference of means on natural logarithm scale of 1.0 – ratio.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 18-10. Analysis of the Ratio of Observed FEV_1 to Observed FVC (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	**n**	**Adj. Mean[a]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]**	**p-Value[c]**
Comparison	1,210	0.770		
Background RH	380	0.766	–0.004 --	0.376
Low RH	237	0.772	0.002 --	0.740
High RH	243	0.774	0.004 --	0.466
Low plus High RH	480	0.773	0.003 --	0.481

[a] Transformed from natural logarithm scale of 1.0 – ratio.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale of 1.0 – ratio.
[c] P-value is based on difference of means on natural logarithm scale of 1.0 – ratio.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin +1)**		
1987 Dioxin	**n**	**Mean[a]**	**R^2**	**Slope (Std. Error)[b]**	**p-Value**
Low	288	0.753	0.018	–0.031 (0.008)	<0.001
Medium	287	0.757			
High	287	0.771			

[a] Transformed from natural logarithm scale of 1.0 – ratio.
[b] Slope and standard error based on natural logarithm of (1.0 – ratio) versus $\log_2$ (1987 dioxin + 1); because of this transformation, a negative slope implies a positive association between the ratio and $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**		
1987 Dioxin	**n**	**Adj. Mean[a]**	**R^2**	**Adjusted Slope (Std. Error)[b]**	**p-Value**
Low	287	0.767	0.218	–0.012 (0.008)	0.161
Medium	286	0.770			
High	287	0.773			

[a] Transformed from natural logarithm scale of 1.0 – ratio.
[b] Slope and standard error based on natural logarithm of (1.0 – ratio) versus $\log_2$ (1987 dioxin + 1); because of this transformation, a negative slope implies a positive association between the ratio and $\log_2$ (1987 dioxin+1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

18.2.2.3.5 Loss of Vital Capacity

No significant relations were observed between group or dioxin and the loss of vital capacity in Models 1 through 3 (Table 18-11(a–f): p>0.11 for each analysis).

Table 18-11. Analysis of Loss of Vital Capacity

(a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Number (%) None	Number (%) Mild	Number (%) Moderate or Severe	Mild vs. None: Est. Relative Risk (95% C.I.)	Mild vs. None: p-Value	Moderate or Severe vs. None: Est. Relative Risk (95% C.I.)	Moderate or Severe vs. None: p-Value
All	***Ranch Hand***	***869***	***792 (91.1)***	***67 (7.7)***	***10 (1.2)***	***0.98 (0.71,1.35)***	***0.885***	***0.71 (0.33,1.53)***	***0.388***
	Comparison	***1,249***	***1,131 (90.6)***	***98 (7.8)***	***20 (1.6)***				
Officer	Ranch Hand	341	312 (91.5)	24 (7.0)	5 (1.5)	1.10 (0.63,1.90)	0.737	1.46 (0.42,5.10)	0.549
	Comparison	494	457 (92.5)	32 (6.5)	5 (1.0)				
Enlisted Flyer	Ranch Hand	151	139 (92.1)	11 (7.3)	1 (0.7)	0.72 (0.33,1.58)	0.413	0.29 (0.03,2.67)	0.277
	Comparison	186	164 (88.2)	18 (9.7)	4 (2.2)				
Enlisted Groundcrew	Ranch Hand	377	341 (90.5)	32 (8.5)	4 (1.1)	1.00 (0.62,1.59)	0.990	0.54 (0.17,1.72)	0.300
	Comparison	569	510 (89.6)	48 (8.4)	11 (1.9)				

(b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Mild vs. None: Adj. Relative Risk (95% C.I.)	Mild vs. None: p-Value	Moderate or Severe vs. None: Adj. Relative Risk (95% C.I.)	Moderate or Severe vs. None: p-Value
All	***0.96 (0.69,1.35)***	***0.832***	***0.67 (0.31,1.47)***	***0.324***
Officer	1.09 (0.62,1.90)	0.768	1.42 (0.40,5.00)	0.586
Enlisted Flyer	0.68 (0.31,1.52)	0.349	0.25 (0.03,2.30)	0.220
Enlisted Groundcrew	1.00 (0.61,1.63)	0.999	0.52 (0.16,1.70)	0.279

Table 18-11. Analysis of Loss of Vital Capacity (Continued)

(c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category Summary Statistics					Analysis Results for Log$_2$ (Initial Dioxin)[a]			
		Number (%)			Mild vs. None		Moderate or Severe vs. None	
Initial Dioxin Category	n	None	Mild	Moderate or Severe	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
Low	160	146 (91.3)	12 (7.5)	2 (1.3)	0.88 (0.67,1.15)	0.345	0.73 (0.31,1.76)	0.489
Medium	161	145 (90.1)	15 (9.3)	1 (0.6)				
High	160	151 (94.4)	8 (5.0)	1 (0.6)				

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

	Analysis Results for Log$_2$ (Initial Dioxin)			
	Mild vs. None		Moderate or Severe vs. None	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
480	0.91 (0.66,1.24)	0.539	1.02 (0.35,2.99)	0.973

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results not adjusted for race, current cigarette smoking, and industrial chemicals exposure because of the sparse number of moderate or severe measurements.

Table 18-11. Analysis of Loss of Vital Capacity (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Number (%) None	Number (%) Mild	Number (%) Moderate or Severe	Mild vs. None: Est. Relative Risk (95% C.I.)[ab]	Mild vs. None: p-Value	Moderate or Severe vs. None: Est. Relative Risk (95% C.I.)[ab]	Moderate or Severe vs. None: p-Value
Comparison	1,211	1,096 (90.5)	97 (8.0)	18 (1.5)				
Background RH	381	344 (90.3)	31 (8.1)	6 (1.6)	1.18 (0.77,1.81)	0.456	1.27 (0.50,3.27)	0.616
Low RH	238	218 (91.6)	18 (7.6)	2 (0.8)	0.89 (0.52,1.51)	0.663	0.52 (0.12,2.28)	0.387
High RH	243	224 (92.2)	17 (7.0)	2 (0.8)	0.75 (0.43,1.29)	0.295	0.46 (0.10,2.00)	0.297
Low plus High RH	481	442 (91.9)	35 (7.3)	4 (0.8)	0.81 (0.54,1.23)	0.325	0.49 (0.16,1.46)	0.199

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Mild vs. None: Adj. Relative Risk (95% C.I.)[a]	Mild vs. None: p-Value	Moderate or Severe vs. None: Adj. Relative Risk (95% C.I.)[a]	Moderate or Severe vs. None: p-Value
Comparison	1,210				
Background RH	380	1.28 (0.82,1.99)	0.284	1.44 (0.54,3.81)	0.468
Low RH	237	0.71 (0.41,1.24)	0.235	0.34 (0.07,1.57)	0.165
High RH	243	0.75 (0.43,1.32)	0.325	0.47 (0.10,2.17)	0.337
Low plus High RH	480	0.73 (0.48,1.12)	0.151	0.40 (0.13,1.25)	0.115

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 18-11. Analysis of Loss of Vital Capacity (Continued)

(g) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED

1987 Dioxin Category Summary Statistics					Analysis Results for Log_2 (1987 Dioxin + 1)			
		Number (%)			Mild vs. None		Moderate or Severe vs. None	
1987 Dioxin Category	n	None	Mild	Moderate or Severe	Est. Relative Risk (95% C.I.)[a]	p-Value	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	288	265 (92.0)	19 (6.6)	4 (1.4)	0.94 (0.79,1.12)	0.480	0.83 (0.53,1.31)	0.430
Medium	287	254 (88.5)	29 (10.1)	4 (1.4)				
High	287	267 (93.0)	18 (6.3)	2 (0.7)				

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS — 1987 DIOXIN — ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin + 1)			
	Mild vs. None		Moderate or Severe vs. None	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
860	0.80 (0.65,1.00)	0.046	0.87 (0.50,1.50)	0.605

[a] Relative risk for a twofold increase in 1987 dioxin.

The Model 4 unadjusted analysis of loss of vital capacity was nonsignificant (Table 18-11(g): p>0.43 for each contrast). After adjusting for covariates, a significant association between a mild loss of vital capacity and 1987 dioxin was revealed (Table 18-11(h): Adj. RR=0.80, p=0.046). The prevalence of a mild loss of vital capacity decreased as 1987 dioxin increased, after accounting for covariate effects. The percentages of participants with a mild loss of vital capacity in the low, medium, and high 1987 dioxin categories were 6.6, 10.1, and 6.3, respectively.

18.2.2.3.6 Obstructive Abnormality

The Model 1 unadjusted and adjusted analyses showed no group difference for obstructive abnormalities when combining all occupations (p>0.23 for each analysis). After stratifying by occupation, both the unadjusted and adjusted analyses revealed a significant difference between Ranch Hand and Comparison officers in the percentage of mild obstructive abnormalities (Table 18-12(a,b): Est. RR=1.38, p=0.034; Adj. RR=1.38, p=0.041, respectively). The percentage of Ranch Hand officers with mild obstructive abnormalities was higher than the percentage of Comparison officers with mild obstructive abnormalities (36.4% vs. 29.8%). No significant differences were noted for any occupation for the contrast of moderate versus no obstructive abnormalities (p>0.36 for all analyses) or for the contrast of severe versus no obstructive abnormalities ($p \geq 0.18$ for all analyses).

Table 18-12. Analysis of Obstructive Abnormality

(a1) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Number (%) None	Mild	Moderate	Severe
All	***Ranch Hand***	***869***	***528 (60.8)***	***276 (31.8)***	***51 (5.9)***	***14 (1.6)***
	Comparison	***1,249***	***790 (63.3)***	***368 (29.5)***	***75 (6.0)***	***16 (1.3)***
Officer	Ranch Hand	341	193 (56.6)	124 (36.4)	19 (5.6)	5 (1.5)
	Comparison	494	316 (64.0)	147 (29.8)	26 (5.3)	5 (1.0)
Enlisted Flyer	Ranch Hand	151	82 (54.3)	49 (32.5)	14 (9.3)	6 (4.0)
	Comparison	186	97 (52.2)	72 (38.7)	12 (6.5)	5 (2.7)
Enlisted Groundcrew	Ranch Hand	377	253 (67.1)	103 (27.3)	18 (4.8)	3 (0.8)
	Comparison	569	377 (66.3)	149 (26.2)	37 (6.5)	6 (1.1)

(a2) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

	Mild vs. None		Moderate vs. None		Severe vs. None	
Occupational Category	Est. Relative Risk (95% C.I.)	p-Value	Est. Relative Risk (95% C.I.)	p-Value	Est. Relative Risk (95% C.I.)	p-Value
All	***1.12 (0.93,1.36)***	***0.237***	***1.02 (0.70,1.48)***	***0.928***	***1.31 (0.63,2.70)***	***0.467***
Officer	1.38 (1.02,1.86)	0.034	1.20 (0.64,2.22)	0.569	1.64 (0.47,5.73)	0.440
Enlisted Flyer	0.81 (0.50,1.28)	0.363	1.38 (0.60,3.15)	0.444	1.42 (0.42,4.82)	0.574
Enlisted Groundcrew	1.03 (0.77,1.39)	0.845	0.72 (0.40,1.30)	0.281	0.75 (0.18,3.00)	0.679

Table 18-12. Analysis of Obstructive Abnormality (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Mild vs. None: Est. Relative Risk (95% C.I.)	Mild vs. None: p-Value	Moderate vs. None: Est. Relative Risk (95% C.I.)	Moderate vs. None: p-Value	Severe vs. None: Est. Relative Risk (95% C.I.)	Severe vs. None: p-Value
All	***1.08 (0.88,1.32)***	***0.449***	***0.97 (0.66,1.44)***	***0.887***	***1.22 (0.57,2.59)***	***0.605***
Officer	1.38 (1.01,1.89)	0.041	1.21 (0.63,2.32)	0.560	1.81 (0.50,6.57)	0.366
Enlisted Flyer	0.79 (0.48,1.29)	0.345	1.36 (0.57,3.23)	0.492	1.27 (0.35,4.58)	0.715
Enlisted Groundcrew	0.96 (0.70,1.32)	0.821	0.65 (0.35,1.22)	0.180	0.69 (0.16,2.87)	0.607

(c1) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category	n	Initial Dioxin Category Summary Statistics Number (%): None	Mild	Moderate	Severe
Low	160	93 (58.1)	52 (32.5)	11 (6.9)	4 (2.5)
Medium	161	94 (58.4)	56 (34.8)	8 (5.0)	3 (1.9)
High	160	121 (75.6)	32 (20.0)	7 (4.4)	0 (0.0)

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(c2) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Analysis Results for Log_2 (Initial Dioxin)[a]					
Mild vs. None		Moderate vs. None		Severe vs. None	
Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
0.79 (0.67,0.93)	0.005	0.87 (0.63,1.20)	0.393	0.53 (0.24,1.21)	0.131

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

(d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)						
	Mild vs. None		Moderate vs. None		Severe vs. None	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
480	0.86 (0.72,1.02)	0.082	0.98 (0.67,1.42)	0.902	0.63 (0.28,1.44)	0.276

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results not adjusted for race, occupation, and industrial chemicals exposure because of the sparse number of severe obstructive abnormalities.

Table 18-12. Analysis of Obstructive Abnormality (Continued)

(e1) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
		Number (%)			
Dioxin Category	**n**	**None**	**Mild**	**Moderate**	**Severe**
Comparison	1,211	767 (63.3)	356 (29.4)	73 (6.0)	15 (1.2)
Background RH	381	218 (57.2)	131 (34.4)	25 (6.6)	7 (1.8)
Low RH	238	134 (56.3)	85 (35.7)	13 (5.5)	6 (2.5)
High RH	243	174 (71.6)	55 (22.6)	13 (5.3)	1 (0.4)
Low plus High RH	481	308 (64.0)	140 (29.1)	26 (5.4)	7 (1.5)

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(e2) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED						
	Mild vs. None		Moderate vs. None		Severe vs. None	
Dioxin Category	**Adj. Relative Risk (95% C.I.)[a]**	**p-Value**	**Adj. Relative Risk (95% C.I.)[a]**	**p-Value**	**Adj. Relative Risk (95% C.I.)**	**p-Value**
Comparison						
Background RH	1.26 (0.98,1.62)	0.071	1.14 (0.70,1.85)	0.595	1.42 (0.57,3.55)	0.453
Low RH	1.38 (1.02,1.86)	0.037	1.03 (0.56,1.92)	0.915	2.37 (0.90,6.24)	0.080
High RH	0.70 (0.50,0.97)	0.031	0.82 (0.44,1.52)	0.533	0.33 (0.04,2.56)	0.291
Low plus High RH	0.98 (0.77,1.24)	0.838	0.92 (0.58,1.47)	0.731	0.88 (0.27,2.90)	0.835

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 18-12. Analysis of Obstructive Abnormality (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED							
		Mild vs. None		Moderate vs. None		Severe vs. None	
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)	p-Value
Comparison	1,210						
Background RH	380	1.21 (0.93,1.58)	0.164	1.22 (0.73,2.04)	0.440	1.64 (0.62,4.34)	0.323
Low RH	237	1.17 (0.85,1.60)	0.338	0.78 (0.40,1.52)	0.459	1.75 (0.62,4.89)	0.289
High RH	243	0.74 (0.52,1.06)	0.096	0.76 (0.39,1.49)	0.429	0.28 (0.03,2.26)	0.232
Low plus High RH	480	0.93 (0.72,1.20)	0.556	0.77 (0.46,1.28)	0.311	0.69 (0.20,2.37)	0.557

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g1) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED					
		1987 Dioxin Category Summary Statistics Number (%)			
1987 Dioxin Category	n	None	Mild	Moderate	Severe
Low	288	168 (58.3)	97 (33.7)	17 (5.9)	6 (2.1)
Medium	287	161 (56.1)	101 (35.2)	20 (7.0)	5 (1.7)
High	287	197 (68.6)	73 (25.4)	14 (4.9)	3 (1.0)

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(g2) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED					
Analysis Results for Log_2 (1987 Dioxin+1)					
Mild vs. None		Moderate vs. None		Severe vs. None	
Est. Relative Risk (95% C.I.)[a]	p-Value	Est. Relative Risk (95% C.I.)[a]	p-Value	Est. Relative Risk (95% C.I.)[a]	p-Value
0.83 (0.75,0.92)	<0.001	0.86 (0.70,1.05)	0.145	0.70 (0.47,1.04)	0.078

[a] Relative risk for a twofold increase in 1987 dioxin.

(h) MODEL 4: RANCH HANDS — 1987 DIOXIN — ADJUSTED						
	Analysis Results for Log_2 (1987 Dioxin+1)					
	Mild vs. None		Moderate vs. None		Severe vs. None	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
860	0.91 (0.80,1.04)	0.177	0.87 (0.67,1.12)	0.269	0.78 (0.50,1.22)	0.272

[a] Relative risk for a twofold increase in 1987 dioxin.

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In each of the unadjusted and adjusted Model 2 analyses, a significant or marginally significant decreased risk of mild obstructive abnormalities for increasing initial dioxin levels was revealed (Table 18-12(c,d): Est. RR=0.79, p=0.005; Adj. RR=0.86, p=0.082, respectively). The percentages of mild obstructive abnormalities in the low, medium, and high initial dioxin categories were 32.5, 34.8, and 20.0, respectively. No significant difference was seen in the moderate versus no obstructive abnormalities contrast or the severe versus no obstructive abnormalities contrast (p>0.13 for all analyses).

The unadjusted Model 3 analysis revealed three significant or marginally significant differences between Ranch Hands and Comparisons in the percentage of participants with mild abnormalities. Ranch Hands in the background dioxin category had a higher percentage of mild obstructive abnormalities than did Comparisons (Table 18-12(e): 34.4% vs. 29.4%, Est. RR=1.26, p=0.071), as did Ranch Hands in the low dioxin category (Table 18-12(e): 35.7% vs. 29.4%, Est. RR=1.38, p=0.037). Ranch Hands in the high dioxin category had a lower percentage of mild obstructive abnormalities than did Comparisons (Table 18-12(e): 22.6% vs. 29.4%, Est. RR=0.70, p=0.031). A marginally significant greater percentage of Ranch Hands in the low dioxin category had a severe obstructive abnormality than did Comparisons (Table 18-12(e): 2.5% vs. 1.2%, Est. RR=2.37, p=0.080). After adjusting for covariates, only the difference in mild obstructive abnormalities between Ranch Hands in the high dioxin category and Comparisons remained marginally significant (Table 18-12(f): Adj. RR=0.74, p=0.096). No significant difference was detected in the moderate versus no obstructive abnormalities contrast (p>0.31 for all analyses).

The unadjusted Model 4 analysis showed a significant or marginally significant decreased risk of mild and severe obstructive abnormalities with increasing 1987 dioxin levels (Table 18-12(g): Est. RR=0.83, p<0.001, for the mild versus no obstructive abnormalities contrast; Est. RR=0.70, p=0.078, for the severe versus no obstructive abnormalities contrast). The percentages of mild obstructive abnormalities in the low, medium, and high 1987 dioxin categories were 33.7, 35.2, and 25.4, respectively. The percentages of severe obstructive abnormalities in the low, medium, and high 1987 dioxin categories were 2.1, 1.7, and 1.0, respectively. After adjusting for covariates, both contrasts became nonsignificant (p>0.17 for each contrast). No significant difference was observed in the moderate versus no obstructive abnormalities contrast (p>0.14 for all analyses).

18.2.3 Longitudinal Analysis

Longitudinal analyses were conducted on the ratio of observed FEV_1 to observed FVC to examine whether changes across time differed with respect to group membership (Model 1), initial dioxin (Model 2), and categorized dioxin (Model 3). Model 4 was not examined in longitudinal analyses because 1987 dioxin, the measure of exposure in these models, changes over time and was not available for all participants for 1982 or 1997. Summary statistics are provided for reference purposes for the 1987 and 1992 examinations. This measurement was not collected for the 1985 follow-up examination.

The longitudinal analysis for the ratio of observed FEV_1 to observed FVC examined the paired difference between the measurements from 1982 and 1997. These paired differences measured the change in the ratio over time. A logarithmic transformation was applied to 1.0 minus this ratio prior to calculating the paired differences for analytic purposes. Each of the three models used in the longitudinal analysis was adjusted for age and the ratio as measured in 1982 (see Chapter 7, Statistical Methods). The analyses of Models 2 and 3 also were adjusted for body fat at the time of the blood measurement of dioxin.

18.2.3.1 Laboratory Examination Variable

18.2.3.1.1 Ratio of Observed FEV_1 to Observed FVC

The Model 1 analysis of the change in the mean ratio of observed FEV_1 to observed FVC revealed a significant difference between Ranch Hands and Comparisons when combining all occupations (Table 18-13(a): difference=–0.005, p=0.048). The Ranch Hand group had a decrease in the mean ratio of 0.057 from 1982 to 1997, whereas the Comparison group showed a decrease of 0.052. Stratifying by occupation showed a marginally significant group difference among the enlisted flyers (difference=–0.014, p=0.072). The Ranch Hand enlisted flyers showed a decrease in the mean ratio of 0.072 between 1982 and 1997, compared to a decrease of 0.058 for the Comparison enlisted flyers.

The Model 2 analysis did not reveal a significant association between the change in the ratio of observed FEV_1 to observed FVC and initial dioxin (p=0.726).

The Model 3 analysis of the change in the ratio of observed FEV_1 to observed FVC revealed a marginally significant difference between the low and high dioxin categories combined and Comparisons (Table 18-13(c): difference=–0.004, p=0.052). The low and high dioxin categories combined had a decrease in the mean ratio of 0.056 between 1982 and 1997, versus a decrease of the mean ratio of 0.052 for the Comparison category.

Table 18-13. Longitudinal Analysis of the Ratio of Observed FEV_1 to Observed FVC

(a) MODEL 1: RANCH HANDS VS. COMPARISONS								
		Mean[a]/(n) Examination						
Occupational Category	Group	1982	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	***Ranch Hand***	***0.817 (817)***	***0.818 (790)***	***0.764 (795)***	***0.760 (817)***	***–0.057***	***–0.005***	***0.048***
	Comparison	***0.816 (973)***	***0.818 (948)***	***0.765 (953)***	***0.764 (973)***	***–0.052***		
Officer	Ranch Hand	0.810 (311)	0.812 (304)	0.755 (306)	0.755 (311)	–0.055	–0.001	0.763
	Comparison	0.813 (380)	0.812 (368)	0.758 (375)	0.760 (380)	–0.054		
Enlisted Flyer	Ranch Hand	0.812 (148)	0.802 (142)	0.746 (145)	0.740 (148)	–0.072	–0.014	0.072
	Comparison	0.806 (143)	0.807 (141)	0.756 (141)	0.748 (143)	–0.058		
Enlisted Groundcrew	Ranch Hand	0.826 (358)	0.829 (344)	0.779 (344)	0.772 (358)	–0.054	–0.006	0.152
	Comparison	0.821 (450)	0.826 (439)	0.775 (437)	0.773 (450)	–0.048		

[a] Transformed from natural logarithm scale of (1 – ratio of observed FEV_1 to observed FVC).
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of natural logarithm of (1 – ratio of observed FEV_1 to observed FVC); results adjusted for natural logarithm of (1 – ratio of observed FEV_1 to observed FVC) in 1982 and age in 1997.

Note: Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 18-13. Longitudinal Analysis of the Ratio of Observed FEV_1 to Observed FVC (Continued)

(b) MODEL 2: RANCH HANDS – INITIAL DIOXIN						
Initial Dioxin Category Summary Statistics					**Analysis Results for Log_2 (Initial Dioxin)[b]**	
	Mean[a]/(n) Examination					
Initial Dioxin	**1982**	**1987**	**1992**	**1997**	**Adjusted Slope (Std. Error)**	**p-Value**
Low	0.816 (154)	0.815 (153)	0.759 (149)	0.757 (154)	0.003 (0.009)	0.726
Medium	0.816 (158)	0.813 (155)	0.763 (155)	0.755 (158)		
High	0.835 (153)	0.842 (148)	0.792 (150)	0.785 (153)		

[a] Transformed from natural logarithm scale of (1 − ratio of observed FEV_1 to observed FVC).
[b] Results based on difference between natural logarithm of (1 − 1997 ratio of observed FEV_1 to observed FVC) and natural logarithm of (1 − 1982 ratio of observed FEV_1 to observed FVC) versus log_2 (initial dioxin); results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of (1 − 1982 ratio of observed FEV_1 to observed FVC), and age in 1997; because of the transformation used, a negative slope implies a positive association between the ratio and log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 18-13. Longitudinal Analysis of the Ratio of Observed FEV_1 to Observed FVC (Continued)

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY							
Dioxin Category	**Mean[a]/(n) Examination 1982**	**1987**	**1992**	**1997**	**Exam. Mean Change[b]**	**Difference of Exam. Mean Change**	**p-Value[c]**
Comparison	0.816 (945)	0.818 (922)	0.765 (926)	0.763 (945)	–0.052		
Background RH	0.810 (346)	0.809 (329)	0.754 (336)	0.752 (346)	–0.059	–0.007	0.486
Low RH	0.819 (229)	0.816 (226)	0.763 (222)	0.758 (229)	–0.061	–0.009	0.109
High RH	0.826 (236)	0.831 (230)	0.780 (232)	0.774 (236)	–0.052	0.000	0.161
Low plus High RH	0.822 (465)	0.823 (456)	0.772 (454)	0.766 (465)	–0.056	–0.004	0.052

[a] Transformed from natural logarithm scale of (1 − ratio of observed FEV_1 to observed FVC).
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of natural logarithm of (1 − 1997 ratio of observed FEV_1 to observed FVC); results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of (1 − 1982 ratio of observed FEV_1 to observed FVC), and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

18.3 DISCUSSION

Although the presence of pulmonary disease is often apparent based on the participant’s history and physical examination, confirmation of the diagnosis and quantification of the degree of pulmonary impairment usually requires collection of the laboratory data analyzed in the current chapter. In addition, because the lung is often involved secondarily in numerous infectious, inflammatory, and neoplastic disorders, the assessment of lung disease should include the type of comprehensive multi-system review conducted in these examinations and reported in other chapters.

Historical information on the occurrence of pulmonary disease must be interpreted with caution in the absence of medical record verification. Many of the cardinal symptoms of lung disease, including dyspnea, chest pain, and exercise intolerance, are common to cardiovascular disease as well, particularly ischemic heart disease, and are misinterpreted frequently as to cause. Wheezing, assumed by the patient to be indicative of asthma, may in fact be reflective of hemodynamic compromise in congestive heart failure. “Pneumonia” and “pneumonitis” are often confused by patients in relating the medical history. Thus, all episodes of pulmonary disease were verified by medical records and only documented occurrences were analyzed.

The physical examination variables studied can provide valuable clues to the presence of pulmonary disease; however, in lacking specificity, these data have limitations in confirming a diagnosis. Wheezes and hyperresonance, for example, will occur in obstructive airway disease in asthma or in emphysema secondary to cigarette use. Dullness to percussion, a finding common to many disorders, will occur in consolidation from atelectasis, infections, pleural thickening, or pleural effusion.

In view of the limitations of the participant's history and physical examination noted above, added emphasis is placed on screening laboratory data in the diagnosis of respiratory disease. The chest x ray, when normal, is highly reliable in excluding pulmonary parenchymal disease, although several exceptions must be recognized. Solitary lesions less than 6 millimeters, miliary granulomatous infection, and early interstitial disease, among others, may be present but not detectable radiographically. Furthermore, it is recognized clinically that the chest x ray is not sensitive to the detection of obstructive airway disease in an early stage. On the other hand, the chest x ray may reveal an early occult malignancy in an asymptomatic patient and afford a rare opportunity for cure.

Spirometry has been used as a clinical tool to measure static lung volumes and to detect respiratory disease for more than a century. Dynamic indices, relating changes in lung volume to time, were first developed more than 50 years ago and, with computerization, have been refined to a high degree of accuracy and reproducibility. To be valid, spirometry requires that particular attention be paid to technician training and to eliciting the full cooperation of the patient. In spirometry, a premium is placed on using identical techniques in longitudinal studies. These factors received special emphasis in this study.

The spirometric indices evaluated in this section, FEV_1 and FVC, are designed to measure lung volume. Height is the principal determinant of static lung volume, as measured by the vital capacity, whereas dynamic flow measurements depend more on physical strength. Accordingly, all indices require correction for height and age. Race-specific variations in spirometric indices, reflective of differences in body habitus, have been well documented and recently summarized (44). Blacks, for example, have FVC and FEV_1 values that average 12 to 15 percent less than Caucasian Americans of comparable height.

In clinical practice, it is convenient to divide respiratory disease into two broad categories: "restrictive" and "obstructive." "Restrictive" disease is characterized by reduced vital capacity as seen in interstitial fibrosis or reduced lung volume consequent to surgical resection. In "obstructive" disease, whether associated with asthma or with cigarette use, the flow-dependent index, FEV_1, is abnormally prolonged.

The analyses of the dependent variable-covariate associations confirm observations that are well established in clinical practice. Lifetime cigarette smoking history was a consistent and highly significant risk factor for the development of bronchitis and, in a dose-response pattern, associated with abnormalities in all of the laboratory indices examined. At each of the AFHS examinations, all nicotine-dependent participants were counseled on smoking cessation. Of interest, over the 15-year course of these examinations, the percentage of nicotine-dependent participants has fallen from 42 percent in 1982 to just under 20 percent in 1997. With advancing age, an increase in respiratory disease was confirmed by history and on physical examination, as was a progressive age-related reduction in the dynamic index of pulmonary function, the FEV_1 and, to a lesser extent, the vital capacity. Because spirometric indices were not corrected for race in this follow-up examination, Blacks were found to have reductions of approximately 10 percent in FVC, FEV_1, and the ratio of observed FEV_1 to observed FVC. Finally, the analyses of body fat confirmed the well recognized reduction in vital capacity and its derived indices associated with obesity.

The analyses of historical variables yielded inconsistent results. Ranch Hands were more likely than Comparisons to have had bronchitis and asthma, whereas the prevalence of pneumonia was greater in Comparisons. In none of the contrasts were the differences significant. Similar to the 1992 examinations, but of unknown cause, Ranch Hand enlisted flyers appeared to be at selective risk relative to Comparisons with respect to the history of bronchitis (27.8% vs. 19.1%). Within this occupational stratum, there are no longer any significant group differences on physical examination or by chest x ray. Further, in none of these analyses was there any relation with the body burden of dioxin.

A significantly increased risk of mild obstructive abnormality was found in Ranch Hand officers. This finding was not present in 1992. The meaning of the finding is uncertain because the risk was not significantly increased in Ranch Hand enlisted groundcrew—the subgroup with the highest dioxin levels. The relation between mild obstructive abnormality in Ranch Hand officers and indicators of herbicide exposure, such as job (pilot, navigator, nonflyer), the number of missions flown, the percentage of missions that were herbicide missions, and reported drinking of herbicide (yes, no) will be summarized in a separate report.

In none of the static and dynamic spirometric indices were any significant group differences defined, nor was there evidence for any adverse effect associated with prior dioxin exposure.

Longitudinal analyses of the ratio of observed FEV_1 to observed FVC confirms the gradual decline in this index associated with age in both the Ranch Hand and Comparison cohorts. Similar to the 1992 results, in the enlisted flyer category, Ranch Hands had a slightly greater reduction in the ratio than did Comparisons, but the difference (−0.072 vs. −0.058) is not physiologically meaningful.

In conclusion, apart from the marginally significant increase in bronchitis in enlisted flyers noted above, the historical, physical examination, and laboratory data analyzed in the current section revealed no evidence for an increase in pulmonary disease in the Ranch Hand cohort relative to Comparisons. The results also confirmed numerous dependent variable-covariate associations documented in previous AFHS examinations.

18.4 SUMMARY

18.4.1 Model 1: Group Analysis

A marginally significant difference in bronchitis was observed between Ranch Hand and Comparison enlisted flyers in unadjusted and adjusted analyses. Ranch Hand enlisted flyers had a higher prevalence of bronchitis than did Comparison enlisted flyers. Ranch Hand officers had a significantly higher prevalence of mild obstructive abnormality than did Comparison officers in both unadjusted and adjusted analyses. All other tests of the association of group and the pulmonary variables were nonsignificant. The results of the group analyses are summarized in Table 18-14.

Table 18-14. Summary of Group Analysis (Model 1) for Pulmonary Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED All	UNADJUSTED Officer	UNADJUSTED Enlisted Flyer	UNADJUSTED Enlisted Groundcrew
Medical Records				
Asthma (D)	NS	NS	ns	NS
Bronchitis (D)	NS	NS	NS*	NS
Pneumonia (D)	ns	ns	NS	ns
Physical Examination				
Thorax and Lung Abnormalities (D)	NS	NS	NS	ns
Laboratory				
X-ray Interpretation (D)	NS	NS	NS	NS
FVC (C)	NS	NS	NS	NS
FEV_1 (C)	ns	ns	ns	NS
Ratio of Observed FEV_1 to Observed FVC (C)[a]	ns	ns	ns	NS
Loss of Vital Capacity (D):				
Mild vs. None	ns	NS	ns	NS
Moderate or Severe vs. None	ns	NS	ns	ns
Obstructive Abnormality (D):				
Mild vs. None	NS	+0.034	ns	NS
Moderate vs. None	NS	NS	NS	ns
Severe vs. None	NS	NS	NS	ns

Note: NS or ns: Not significant (p>0.10).
NS*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis.
[a]Difference of means negative considered adverse for this variable.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Variable	ADJUSTED All	ADJUSTED Officer	ADJUSTED Enlisted Flyer	ADJUSTED Enlisted Groundcrew
Medical Records				
Asthma (D)	NS	NS	ns	NS
Bronchitis (D)	NS	NS	NS*	NS
Pneumonia (D)	ns	ns	NS	ns
Physical Examination				
Thorax and Lung Abnormalities (D)	ns	NS	ns	ns
Laboratory				
X-ray Interpretation (D)	NS	NS	NS	NS
FVC (C)	NS	NS	NS	NS
FEV_1 (C)	NS	NS	ns	NS
Ratio of Observed FEV_1 to Observed FVC (C)[a]	ns	ns	ns	NS

Table 18-14. Summary of Group Analysis (Model 1) for Pulmonary Variables (Ranch Hands vs. Comparisons) (Continued)

Variable	ADJUSTED All	Officer	Enlisted Flyer	Enlisted Groundcrew
Loss of Vital Capacity (D):				
Mild vs. None	ns	NS	ns	NS
Moderate or Severe vs. None	ns	NS	ns	ns
Obstructive Abnormality (D):				
Mild vs. None	NS	+0.041	ns	ns
Moderate vs. None	ns	NS	NS	ns
Severe vs. None	NS	NS	NS	ns

Note: NS or ns: Not significant (p>0.10).
NS*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis.
[a]Difference of means negative considered adverse for this variable.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

18.4.2 Model 2: Initial Dioxin Analysis

The results of the tests of association between the pulmonary variables and initial dioxin are summarized in Table 18-15. For the unadjusted analysis of pneumonia, a significant decrease in pneumonia was found as initial dioxin increased. After covariate adjustment, the association was no longer significant. The ratio of the observed FEV_1 to the observed FVC significantly increased as initial dioxin increased, but this association was also nonsignificant after adjustment for covariates. The prevalence of a mild obstructive abnormality significantly decreased as initial dioxin increased in the unadjusted analysis. This association was marginally significant after adjustment for covariates. All other tests of association with initial dioxin were nonsignificant.

Table 18-15. Summary of Initial Dioxin Analysis (Model 2) for Pulmonary Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Asthma (D)	NS	NS
Bronchitis (D)	NS	NS
Pneumonia (D)	ns*	ns
Physical Examination		
Thorax and Lung Abnormalities	NS	NS
Laboratory		
X-ray Interpretation (D)	ns	ns
FVC (C)	NS	ns
FEV_1 (C)	NS	NS

Table 18-15. Summary of Initial Dioxin Analyses (Model 2) for Pulmonary Variables (Ranch Hands Only) (Continued)

Variable	Unadjusted	Adjusted
Ratio of Observed FEV_1 to Observed FVC (C)[a]	–0.023	ns
Loss of Vital Capacity (D):		
Mild vs. None	ns	ns
Moderate or Severe vs. None	ns	NS
Obstructive Abnormality (D):		
Mild vs. None	–0.005	ns*
Moderate vs. None	ns	ns
Severe vs. None	ns	ns

Note: NS or ns: Not significant (p>0.10).
ns*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
–: Relative risk <1.00 for discrete analysis; slope negative for continuous analysis.
[a] Positive slope considered adverse for this variable; a negative slope implies an increase in the ratio because of the data transformation used.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

18.4.3 Model 3: Categorized Dioxin Analysis

The results of the categorized dioxin analysis of the pulmonary variables are summarized in Table 18-16. Ranch Hands in the background dioxin category showed a marginally significant increase in bronchitis relative to Comparisons in the adjusted analysis. For the unadjusted and adjusted analyses of the x-ray interpretation, the background Ranch Hands exhibited a significantly higher percentage of abnormalities on the x ray than Comparisons. Unadjusted analyses revealed a higher prevalence of a mild obstructive abnormality for Ranch Hands in the background and low dioxin categories than for Comparisons. These differences between Ranch Hands and Comparisons became nonsignificant after adjustment for covariates. Ranch Hands in the high dioxin category had a significantly smaller prevalence of a mild obstructive abnormality than did Comparisons without adjustment for covariates. The prevalence was marginally significant after adjustment for covariates. Unadjusted analyses revealed a marginally higher prevalence of a severe obstructive abnormality between Ranch Hands in the low dioxin category and Comparisons. This difference between Ranch Hands and Comparisons became nonsignificant after adjustment for covariates.

Table 18-16. Summary of Categorized Dioxin Analysis (Model 3) for Pulmonary Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
Asthma (D)	NS	NS	NS	NS
Bronchitis (D)	NS	NS	NS	NS
Pneumonia (D)	ns	NS	ns	ns
Physical Examination				
Thorax and Lung Abnormalities (D)	ns	NS	NS	NS
Laboratory				
X-ray Interpretation (D)	+0.013	NS	ns	ns
FVC (C)	NS	ns	NS	ns
FEV_1 (C)	ns	ns	NS	ns
Ratio of Observed FEV_1 to Observed FVC (C)[a]	ns	ns	NS	NS
Loss of Vital Capacity (D):				
Mild vs. None	NS	ns	ns	ns
Moderate or Severe vs. None	NS	ns	ns	ns
Obstructive Abnormality (D):				
Mild vs. None	NS*	+0.037	–0.031	ns
Moderate vs. None	NS	NS	ns	ns
Severe vs. None	NS	NS*	ns	ns

Note: NS or ns: Not significant (p>0.10).
NS*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis.
–: Relative risk < 1.00 for discrete analysis.
[a] Difference of means negative considered adverse for this variable.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
Asthma (D)	NS	NS	NS	NS
Bronchitis (D)	NS*	ns	NS	NS
Pneumonia (D)	ns	ns	ns	ns
Physical Examination				
Thorax and Lung Abnormalities (D)	ns	NS	NS	NS
Laboratory				
X-ray Interpretation (D)	+0.004	NS	ns	ns

Table 18-16. Summary of Categorized Dioxin Analysis (Model 3) for Pulmonary Variables (Ranch Hands vs. Comparisons) (Continued)

	ADJUSTED			
Variable	**Background Ranch Hands vs. Comparisons**	**Low Ranch Hands vs. Comparisons**	**High Ranch Hands vs. Comparisons**	**Low plus High Ranch Hands vs. Comparisons**
FVC (C)	ns	NS	NS	NS
FEV_1 (C)	ns	NS	NS	NS
Ratio of Observed FEV_1 to Observed FVC (C)[a]	ns	NS	NS	NS
Loss of Vital Capacity (D):				
Mild vs. None	NS	ns	ns	ns
Moderate or Severe vs. None	NS	ns	ns	ns
Obstructive Abnormality (D):				
Mild vs. None	NS	NS	ns*	ns
Moderate vs. None	NS	ns	ns	ns
Severe vs. None	NS	NS	ns	ns

Note: NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis.
[a] Difference of means negative considered adverse for this variable

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

18.4.4 Model 4: 1987 Dioxin Level Analysis

The adjusted analysis of thorax and lung abnormalities revealed a marginally significant association between the prevalence of abnormalities and 1987 dioxin. The prevalence of abnormalities increased as 1987 dioxin increased. The unadjusted and adjusted analyses of the x-ray interpretation each exhibited a significant decrease in the prevalence of an x ray with abnormalities with an increase in 1987 dioxin. The ratio of the observed FEV_1 to the observed FVC significantly increased as 1987 dioxin increased, but this association was nonsignificant after adjustment for covariates. The adjusted analysis for a mild loss of vital capacity revealed a significant decrease in the loss of vital capacity as 1987 dioxin increased. The prevalence of a mild obstructive abnormality significantly decreased as 1987 dioxin increased in the unadjusted analysis. This association was nonsignificant after adjustment for covariates. The prevalence of a severe obstructive abnormality showed a marginally significant decrease as 1987 dioxin increased, but this association was also nonsignificant after adjustment for covariates. The results for the variables described above, as well as the other pulmonary variables, are summarized in Table 18-17.

Table 18-17. Summary of 1987 Dioxin Analysis (Model 4) for Pulmonary Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Asthma (D)	NS	NS
Bronchitis (D)	ns	ns
Pneumonia (D)	ns	ns
Physical Examination		
Thorax and Lung Abnormalities (D)	NS	NS*
Laboratory		
X-ray Interpretation (D)	–0.015	–0.015
FVC (C)	ns	NS
FEV_1 (C)	NS	NS
Ratio of Observed FEV_1 to Observed FVC (C)[a]	–<0.001	ns
Loss of Vital Capacity (D):		
Mild vs. None	ns	–0.046
Moderate or Severe vs. None	ns	ns
Obstructive Abnormality (D):		
Mild vs. None	–<0.001	ns
Moderate vs. None	ns	ns
Severe vs. None	ns*	ns

Note: NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
–: Relative risk <1.00 for discrete analysis; slope negative for continuous analysis.
[a] Positive slope considered adverse for this variable; a negative slope implies an increase in the ratio because of the data transformation used.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

18.5 CONCLUSION

To assess the pulmonary status for the 1997 AFHS follow-up examination, verified histories of asthma, bronchitis, and pneumonia were studied. A composite measure of thorax and lung abnormalities, as determined from the presence of asymmetrical expansion, hyperresonance, dullness, wheezes, rales, chronic obstructive pulmonary diseases, or the physician's assessment of abnormality, also was analyzed. A routine chest x ray and five measures of pulmonary function using standard spirometric techniques were analyzed.

Few significant increases in adverse pulmonary conditions were observed for Ranch Hands, and isolated and inconsistent associations between the pulmonary endpoints and increased dioxin were seen. No consistent pattern or dose-response relation was evident. Ranch Hands in the background dioxin category exhibited a significantly higher percentage of abnormalities on the chest x-ray than did Comparisons. Ranch Hand officers had a significantly higher prevalence of mild obstructive abnormality than did

Comparison officers; the corresponding contrast was not significant in 1992, and officers were not analyzed as a separate stratum in 1982, 1985, or 1987.

In summary, analysis of historical, physical examination, and laboratory data revealed no relation between dioxin levels and pulmonary disease; however, the prevalence of mild obstructive abnormalities was significantly increased in Ranch Hand officers. The meaning of this finding is unclear because the risk was not significantly increased in Ranch Hand enlisted groundcrew—the military occupation with the highest dioxin levels.

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